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(54) Title: HIGH THROUGHPUT SCREEN FOR INHIBITORS OF FATTY ACID BIOSYNTHESIS IN BACTERIA

(57) Abstract: Methods for identifying compounds that are inhibitors of bacterial fatty acid biosynthesis are disclosed. Such compounds can be used as lead compounds in methods for preparing antibacterial agents for treating bacterial infections (e.g., in humans, animals, and plants). Inhibitors of bacterial fatty acid synthesis can also be tested for their ability to inhibit synthesis of acylated homoserine lactones. Compounds that inhibit synthesis of acylated homoserine lactones can be used as inhibitors of bacterial virulence. The disclosed methods allow for high throughput screening of libraries of test compounds.

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INTERNATIONAL SEARCH REPORT

national Application No

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A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C12Q1/68 A61K31/00 A61P31/04

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, MEDLINE, EMBASE, CANCERLIT, LIFESCIENCES, BIOSIS, SEQUENCE SEARCH

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	HOANG TUNG T ET AL: "Characterization of Pseudomonas aeruginosa enoyl-acyl carrier protein reductase (FabI): A target for the antimicrobial triclosan and its role in acylated homoserine lactone synthesis." JOURNAL OF BACTERIOLOGY, vol. 181, no. 17, 1999, pages 5489-5497, XP002194160 ISSN: 0021-9193 abstract --- -/--	10-16, 20,21, 23-25, 29-34, 37-39

☒ Further documents are listed in the continuation of box C.☐ Patent family members are listed in annex.

* Special categories of cited documents:

A document defining the general state of the art which is not considered to be of particular relevance

E earlier document but published on or after the international filing date

L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

O document referring to an oral disclosure, use, exhibition or other means

P document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

Z document member of the same patent family

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INTERNATIONAL SEARCH REPORT

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	VAL DALE L ET AL: "In vivo evidence that S-adenosylmethionine and fatty acid synthesis intermediates are the substrates for the LuxI family of autoinducer synthases." JOURNAL OF BACTERIOLOGY, vol. 180, no. 10, May 1998 (1998-05), pages 2644-2651, XP000857478 ISSN: 0021-9193 abstract	10-16, 20,21, 23-25, 29-34, 37-39
A	----- HOURDOU M-L ET AL: "SPECIFIC INHIBITION OF ITURIN BIOSYNTHESIS BY CERULENIN" CANADIAN JOURNAL OF MICROBIOLOGY, vol. 36, no. 3, 1990, pages 164-168, XP001053691 ISSN: 0008-4166	
A	----- KUNST F ET AL: "The complete genome sequence of the Gram-positive bacterium Bacillus subtilis." NATURE (LONDON), vol. 390, no. 6657, 20 November 1997 (1997-11-20), pages 249-256, XP000919353 ISSN: 0028-0836 EMBL (online database) SEQ. IDs.: BSUB0006, BSUB0007, BSUB0009 and BSUB0021 the whole document -----	

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Present claims 1-3, 5-8, 17-19, 22, 26, 27, 35 and 36 relate to methods for determining and preparing a test compound which is an inhibitor of bacterial fatty acid biosynthesis (FAB)/antibacterial agent/inhibitor of bacterial virulence, by using a promoter, the activity of which is increased in the presence of a compound that inhibits FAB. The claims cover all promoters having this characteristic or property, whereas the application provides support within the meaning of Article 5 PCT and/or disclosure within the meaning of Article 6 PCT for only a very small proportion of such promoters. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Consequently, the search has been carried out for those parts of the claims which appear to be supported and disclosed, namely those parts relating to PyhFB, PylpC, PyydK and PyjaXY promoters disclosed mentioned in the description at page 13.

Present claims 16, 20, 23, 24, 34, 37 and 38 relate to compounds(=inhibitors of bacterial FAB/antibacterial agents/inhibitors of bacterial virulence) and compositions comprising them, defined by reference to a desirable characteristic or property, namely by being detectable by the method(s) claimed in the present application. The claims cover all compounds(=inhibitors of bacterial FAB/antibacterial agents/inhibitors of bacterial virulence) and compositions comprising them having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such compounds(=inhibitors of bacterial FAB/antibacterial agents/inhibitors of bacterial virulence) and compositions comprising them. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely cerulenin and triclosan, mentioned in the description at page 6.

Claims 10-15, 21, 25, 29-33 and 39 are directed to a method of treatment of the human/animal body. Normally the search would be based and performed on the alleged effects of the compounds. However, considering the shortcomings, especially the lack of conciseness mentioned above, the search has been limited to those parts of the claims which appear to be clear, supported and disclosed, namely cerulenin and triclosan, mentioned in the description at page 6.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

receipt of the search report or during any Chapter II procedure.

